

CLAIMS

What is claimed is:

1. A method for increasing the size of a bone growth plate in abnormal bone
5 comprising treating the bone with an effective amount of at least one natriuretic peptide, or variants thereof.
2. The method according to claim 1 wherein said at least one natriuretic peptide is a CNP.
3. The method according to claim 1 wherein said at least one natriuretic
10 peptide is a CNP variant according to SEQ ID NO:5 having amino acid sequence Cys-Phe-Gly-Xaa-Xbb-Xcc-Asp-Arg-Ile-Gly-Xdd-Xee-Ser-Xff-Xgg-Gly-Cys wherein Xaa=Leu, Ile, Val; Xbb=Lys, Leu, Met; Xcc=Leu, Ile, Ala, Val; Xdd=Ser, Ala, Gly, Thr, Asn; Xee=Met, Ala, Trp, His, Lys, Ser, Gly; Xff=Gly, Lys, Ala, Leu; Xgg=Leu, Met.
4. The method according to claim 1 wherein said at least one natriuretic
15 peptide is according to any one of SEQ ID NOs:1-4.
5. The method according to claim 4 wherein said at least one natriuretic peptide is a BNP.
6. The method according to claim 1 further comprising inhibiting the natriuretic peptide clearance receptor.
- 20 7. The method according to claim 1 further comprising an inhibitor of the neutral endopeptidase 24.11.
8. The method according to claim 7 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatril.
9. The method according to claim 7 wherein the step of administering an
25 inhibitor of neutral endopeptidase is performed simultaneously with the step of administering an effective amount of at least one natriuretic peptide.
10. The method according to claim 1 further comprising an inhibitor of tyrosine kinase.

11. The method according to claim 1 wherein said at least one natriuretic peptide is fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein.
12. The method according to claim 10 wherein the carrier protein fusion protein comprises growth hormone.
13. The method according to claim 1 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.
14. The method according to claim 1 wherein the bone is a limb bone.
15. The method according to claim 14 wherein the limb bone is an achondroplastic bone.
16. A method for elongation of an abnormal bone, comprising treating the bone with an effective amount of at least one natriuretic peptide, or variants thereof.
17. The method according to claim 16 wherein said at least one natriuretic peptide is a CNP.
18. The method according to claim 16 wherein said at least one natriuretic peptide is a CNP variant according to SEQ ID NO:5 having amino acid sequence Cys-Phe-Gly-Xaa-Xbb-Xcc-Asp-Arg-Ile-Gly-Xdd-Xee-Ser-Xff-Xgg-Gly-Cys wherein Xaa=Leu, Ile, Val; Xbb=Lys, Leu, Met; Xcc=Leu, Ile, Ala, Val; Xdd=Ser, Ala, Gly, Thr, Asn; Xee=Met, Ala, Trp, His, Lys, Ser, Gly; Xff=Gly, Lys, Ala, Leu; Xgg=Leu, Met.
19. The method according to claim 16 wherein said at least one natriuretic peptide is according to any one of SEQ ID NOs:1-4.
20. The method according to claim 19 wherein said at least one natriuretic peptide is a BNP.
21. The method according to claim 16 further comprising inhibiting the natriuretic peptide clearance receptor.

22. The method according to claim 16 further comprising an inhibitor of the neutral endopeptidase 24.11.

23. The method according to claim 22 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatri.

5 24. The method according to claim 22 wherein the step of administering an inhibitor of neutral endopeptidase is performed simultaneously with the step of administering an effective amount of at least one natriuretic peptide.

25. The method according to claim 16 further comprising an inhibitor of tyrosine kinase.

10 26. The method according to claim 16 wherein said at least one natriuretic peptide is a natriuretic peptide fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein.

27. The method according to claim 26 wherein the carrier protein comprises growth hormone.

15 28. The method according to claim 16 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.

29. The method according to claim 16 wherein the bone is a limb bone.

20 30. The method according to claim 16 wherein the limb bone is an achondroplastic bone.

31. A pharmaceutical composition for bone elongation or treating skeletal dysplasias comprising at least one natriuretic peptide or variants thereof and a carrier or excipient.

25 32. The pharmaceutical composition according to claim 31 wherein said at least one natriuretic peptide is a CNP.

33. The pharmaceutical composition according to claim 31 wherein said at least one natriuretic peptide is a CNP variant according to SEQ ID NO:5 having amino acid

sequence Cys-Phe-Gly-Xaa-Xbb-Xcc-Asp-Arg-Ile-Gly-Xdd-Xee-Ser-Xff-Xgg-Gly-Cys wherein Xaa=Leu, Ile, Val; Xbb=Lys, Leu, Met; Xcc=Leu, Ile, Ala, Val; Xdd=Ser, Ala, Gly, Thr, Asn; Xee=Met, Ala, Trp, His, Lys, Ser, Gly; Xff=Gly, Lys, Ala, Leu; Xgg=Leu, Met.

5 34. The pharmaceutical composition according to claim 31 wherein said at least one natriuretic peptide is according to any one of SEQ ID NOs:1-4.

 35. The pharmaceutical composition according to claim 34 wherein said at least one natriuretic peptide is a BNP.

 36. The pharmaceutical composition according to claim 31 further comprising
10 an inhibitor of the natriuretic peptide clearance receptor.

 37. The pharmaceutical composition according to claim 31 further comprising an inhibitor of the neutral endopeptidase 24.11.

 38. The pharmaceutical composition according to claim 37 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatril.

15 39. The pharmaceutical composition according to claim 31 further comprising an inhibitor of tyrosine kinase.

 40. The pharmaceutical composition according to claim 31 wherein said at least one natriuretic peptide is a natriuretic peptide fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein.

20 41. The pharmaceutical composition according to claim 40 wherein the carrier protein comprises growth hormone.

 42. The pharmaceutical composition according to claim 31 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.

25 43. The pharmaceutical composition according to claim 31 wherein the bone is a limb bone.

44. The pharmaceutical composition according to claim 43 wherein the limb bone is an achondroplasiac bone.

45. A method for treatment of skeletal dysplasias comprising the step of administering to a patient a therapeutically effective amount of at least one natriuretic peptide.

46. The method according to claim 45 wherein said at least one natriuretic peptide is a CNP.

47. The method according to claim 45 wherein said at least one natriuretic peptide is a CNP variant according to SEQ ID NO:5 having amino acid sequence Cys-Phe-Gly-Xaa-Xbb-Xcc-Asp-Arg-Ile-Gly-Xdd-Xee-Ser-Xff-Xgg-Gly-Cys wherein Xaa=Leu, Ile, Val; Xbb=Lys, Leu, Met; Xcc=Leu, Ile, Ala, Val; Xdd=Ser, Ala, Gly, Thr, Asn; Xee=Met, Ala, Trp, His, Lys, Ser, Gly; Xff=Gly, Lys, Ala, Leu; Xgg=Leu, Met.

48. The method according to claim 45 wherein said at least one natriuretic peptide is according to any one of SEQ ID NOs:1-4.

49. The method according to claim 48 wherein said at least one natriuretic peptide is a BNP.

50. The method according to claim 45 further comprising inhibiting the natriuretic peptide clearance receptor.

51. The method according to claim 45 further comprising an inhibitor of neutral endopeptidase 24.11 with an inhibitor.

52. The method according to claim 49 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatril.

53. The method according to claim 45 wherein the step of administering to the patient an inhibitor of neutral endopeptidase 24.11 is performed simultaneously with the step of administering to a patient an effective amount of at least one natriuretic peptide.

54. The method according to claim 45 further comprising administering to the patient an inhibitor of tyrosine kinase.

55. The method according to claim 45 wherein said at least one natriuretic peptide is a natriuretic peptide fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein.

56. The method according to claim 55 wherein the carrier protein fusion protein
5 comprises growth hormone.

57. The method according to claim 45 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.

58. The method according to claim 45 wherein the bone is a limb bone.

10 59. The method according to claim 58 wherein the limb bone is an achondroplasiac bone.

60. A composition for treatment of skeletal dysplasias comprising natriuretic peptide secreting cells.

15 61. The composition of claim 60 wherein the secreted cells are encapsulated within an inert matrix.

62. The composition of claim 60 comprising natriuretic peptide secreting cells encapsulated within an alginate-polylysine-alginate complex and a carrier thereof.

63. A method for treating skeletal dysplasias comprising transplanting or implanting to a patient in need thereof natriuretic peptide secreting cells.

20 64. The method of claim 63 wherein the natriuretic peptide secreting cells are transplanted or implanted to the site of the lesion.

65. The method of claim 63 wherein the natriuretic peptide secreting cells are encapsulated within an inert matrix.

25 66. The method of claim 63 wherein the natriuretic peptide secreting cells are encapsulated within an alginate-polylysine-alginate complex.